

***Remarks***

***Status of the Claims***

The amendments to the claims are supported throughout the specification and at least by the original-filed claims of the application.

***Priority Claim***

On April 22, 2002, Applicants submitted an amendment to the specification solely to perfect the priority claim. The Amendment of April 22, 2002 was not intended as a response to the outstanding office action. Therefore, Applicants respectfully submit that issuance of an Advisory Action was inappropriate and that the Examiner should fully consider the amendments and remarks presented in this Reply After Final.

Because the amendment of April 22, 2002 was not entered, Applicants have again submitted a similar amendment and request its entry. The amendment amends and perfects the priority statement made in the reply of September 26, 2001 that was not entered.

In both the Advisory Action and the Office Action of March 12, 2002, the Examiner raised the issue of new matter issue as related to the priority claim and U.S. Application 09/759,292. Applicants respectfully disagree because no new matter has been entered.

U.S. Application No. 09/759,292 - hereinafter the '292 application is the non-provisional application number for U.S. Provisional Application No. 60/115,920 - hereinafter the '920 application. Reference was made to the '920 provisional application at page 1, line 6 of the originally filed application. Applicants petitioned and were granted the conversion of the provisional application to a non-provisional application. Relevant information concerning the request for and granting of the petition is provided as **Exhibit A**. Therefore reference to the '292 application is not new matter and further since the '920 application was already incorporated by reference, by implication so was the '292 application.

For all of the above reasons, no new matter has been added to the application and the amendment should be entered.

***Claim Rejections Under 35 USC §112, Second Paragraph***

In the Office Action mailed March 12, 2002, the Examiner rejected claims 22, 23, 47 and 99 under 35 USC §112, second paragraph for allegedly being indefinite. Applicants respectfully traverse this rejection.

Applicants have amended claims 22 and 47 as suggested by the Examiner. Therefore, the rejection as it pertains to these claims is moot.

The Examiner rejected claim 23 as indefinite for the recitation of "said deficient adenovirus gene." Applicants disagree. Claim 23 is dependent on claim 22 that recites "a

deficient adenovirus gene." Thus, there is appropriate antecedent basis for "said deficient adenovirus gene" and the language of claim 23 would be clear to one of skill in the art. Further, it is clear from the claim language that at least the complementation of "said deficient adenovirus gene" is under control of an inducible promoter. Therefore, this rejection should be removed.

The Examiner rejected claim 99 as vague and indefinite because of the recitation "biologically active fragment." It is further noted that "the skilled artisan would not be able to identify such a fragment without some teaching based on the structural and functional characteristics of the fragments." Applicants respectfully disagree for several reasons.

First, Applicants still maintain that the term "biologically active fragment" would be understood by one of skill in the art based on the commonly accepted understanding of the recitation. In other words, the phrase would mean a fragment having biological activity similar to, but not necessarily identical to that of the complete molecule.

Second, the Examiner's reference to "structure and function" is not believed to have anything, whatsoever, to do with a §112, second paragraph rejection. If the Applicants are incorrect in this assumption, they respectfully request the Examiner to provide an appropriate citation to support the rejection under §112, second paragraph, for reasons based on structure and function. Otherwise, the rejection of this claim should be withdrawn.

Based on all of the above, the rejections have either been overcome or rendered moot. Therefore, the rejection of the claims under 35 USC §112, second paragraph should be withdrawn.

***Rejection of Claims 1 and 11 Under 35 USC §102(b).***

In the Office Action mailed March 12, 2002, the Examiner rejected claim 1 and 11 under 35 USC §102(b) as allegedly being anticipated by Logan *et al.*, (*Proc. Natl. Acad. Sci.* 81:3655-3659, 1994 - hereinafter "Logan") or in the alternative Sheay *et al.*, (*Biotechniques* 15:856-862, 1993 - hereinafter "Sheay"). Applicants respectfully traverse this rejection, however, solely in an effort to expedite prosecution, claim 1 was amended to remove reference to "partial TPL exon 1." Additionally claims 2-6 and 12 have been amended as suggested by the Examiner.

Applicants were fully aware of Logan and Sheay as noted in the specification at page 66, third full paragraph. Specifically Applicants stated that:

The adenovirus tripartite leader sequence, present at the 5' end of *all* major late adenoviral mRNAs as described by Logan . . . [is] also referred to as a 'partial TPL' since it contains a partial exon 1, corresponding to . . . (the 3' end of the first leader segment) . . .

(Emphasis added). Applicants' claims are *not* anticipated by cited art referring to a "partial" TPL.

Applicants have amended claims 2-6 and 12 as the Examiner has suggested to be independent and include limitations from claim 1. They have, however, only removed reference to the "partial TPL exon 1" from claim 1. Additionally, they have added new

claim 100 which is supported by original claim 1 and recites that all three TPL exons are the same. Such subject matter is not anticipated by the cited art.

Based on all the above, the rejection of the claims under 102(b) is either overcome or obviated and the rejection should be withdrawn.

***Objection to the Claims***

In the Office Action at page 4, the Examiner objected to claims 2-10, 12-21 and 69 as being dependent upon a rejected base claim. Applicants have amended claims 2, 3, 5, 6 and 12 to be independent claims as suggested by the Examiner. Therefore, claims 2, 3, 5, 6 and 12 and those claims dependent thereon are now allowable and the objection to claims is moot and should be withdrawn.

***Conclusion***

The amendments to the claims and specification neither add new matter nor raise new issues for examination and do not result in any net addition of the claims. Therefore, Applicants respectfully request that the Amendments set out above be entered into the captioned application.

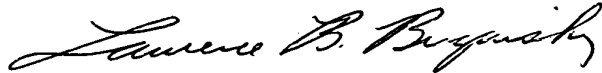
All of the stated grounds of objection and rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the

outstanding Office Action and, as such the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (202) 371-2589.

Prompt and favorable consideration is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Lawrence B. Bugaisky  
Attorney for Applicants  
Registration No. 35,086

Date: September 12, 2002  
1100 New York Avenue, N.W.  
Suite 600  
Washington, D.C. 20005-3934  
(202) 371-2600

**Version with markings to show changes made**

The paragraph beginning at page 1, line 4 was amended as follows:

This application is a continuation-in-part of U.S. Application 09/423,783, filed [June 26, 2000] November 12, 1999 which is [a] the U.S. National [Phase] Stage [application based on International] of PCT Application PCT/EP97/05251, filed September 24, 1997 which [is a continuation-in-part] claims the benefit of the filing date of U.S. Application No. 08/719,806, filed September 25, 1996. [The current] This application is also a continuation-in-part of U.S. Application No. 09/795,292 filed January 14, 1999 (converted to a U.S. Non-Provisional Application from U.S. Provisional Application No. 60/115,920, filed January 14, 1999) which is a continuation-in-part of [is a U.S. National Phase application based on International Application] PCT/EP97/05251, filed September 24, 1997 which [is a continuation-in-part of ] claims the benefit of the filing date of U.S. Application No. 08/719,806, filed September 25, 1996. The contents of each application are incorporated herein by reference.

***In the Claims:***

Claim 1 was amended as follows:

1. (Amended) An isolated nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, [partial TPL exon 1,] complete TPL exon 2 and complete TPL exon 3.

Claim 2 was amended as follows:

2. (Amended) [The isolated nucleic acid molecule of claim 1,] An isolated nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon wherein said TPL nucleotide sequence is operatively linked to an intron containing an RNA processing signal.

Claim 3 was amended as follows:

3. (Amended) [The isolated nucleic acid molecule of claim 1] An isolated nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence wherein said TPL nucleotide sequence consists essentially of complete TPL exon 1 operatively linked to complete TPL exon 2 operatively linked to complete TPL exon 3.

Claim 4 was amended as follows:.

4. (Amended) [The isolated nucleic acid molecule of claim 1] An isolated nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon wherein said intron is native adenovirus intron 1.



Claim 5 was amended as follows:

5. (Amended) [The isolated nucleic acid molecule of claim 1] An isolated nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence wherein said TPL nucleotide sequence is shown in SEQ ID NO: 32.

Claim 6 was amended as follows:

6. (Amended) [The isolated nucleic acid molecule of claim 1] An isolated nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon further comprising a promoter and a nucleic acid sequence which encodes an adenoviral structural protein, operatively linked to said promoter and said TPL sequence.

Claim 12 was amended as follows:

12. (Amended) An adenovirus vector packaging cell line comprising:  
i) a stably integrated nucleic acid molecule [of claim 1], comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon wherein said TPL nucleotide, and

ii) an operatively-linked promoter and a nucleic acid sequence which encodes an adenovirus structural protein,

wherein said TPL sequence consists essentially of a first TPL exon operatively linked to a complete second TPL exon operatively linked to a complete third TPL exon.

Claim 21 was amended as follows.

21. (Amended) The cell line of claim [20] 12 wherein said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome.

Claim 22 was amended as follows:

22. (Amended) The cell line of claim 21 wherein said cell line [further produces an adenovirus protein and thereby complements a deficient adenovirus gene in said vector genome, and wherein said cell line complements] expresses an adenovirus early protein gene and a fiber gene.

Claim 23 was amended as follows.

23. (Amended) The cell line of claim claim [22] 21 wherein [the] deletion of said deficient adenovirus gene is complemented by the expression of said gene under the control of an inducible promoter.

Claim 47 was amended as follows:

47. (Amended) The method of claim [46] 41 wherein said nucleic acid molecule is a nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide

sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and said molecule further comprises a sequence encoding adenovirus fiber protein.